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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,249	12/17/2001	Manuel Vega	37851-911	7196

20985 7590 06/15/2005

FISH & RICHARDSON, PC  
12390 EL CAMINO REAL  
SAN DIEGO, CA 92130-2081

EXAMINER

MAHATAN, CHANNING

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/022,249	<b>Applicant(s)</b> VEGA ET.AL	
	<b>Examiner</b> Channing S. Mahatan	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2005.  
 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-33 and 42-44 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 1-33 and 42-44 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☒ The drawing(s) filed on 22 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) ☐ All b) ☐ Some \* c) ☐ None of:  
 1. ☐ Certified copies of the priority documents have been received.  
 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
 \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>3 Sheets</u> | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### *APPLICANTS' ARGUMENTS*

Applicants' arguments, filed 14 March 2005, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### *CLAIMS UNDER EXAMINATION*

Claims herein under examination are claims 1-33 and 42-44. Claims 34-41 have been canceled.

### **Claims Rejected Under 35 U.S.C. § 112**

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### *NEW MATTER*

Claim 17 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17 is rejected under 35 U.S.C. § 112 1<sup>st</sup> paragraph. Claim 17 has been amended to recited "where an optimized lead comprises two or more hit positions" which is considered new

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matter. Applicants have indicated in the '*RESPONSE*', filed 14 March 2005, support for this amendment can be found on page 34, line 26 to page 35, line 26 which states the following:

“Once the active site(s) (the HITS) has(ve) been identified, those amino acids either at or surrounding the active sites, such as within 1, 2, 3, . . . 10, 20 or any selected regions, as the unitary elements of exchange and generate diversity either at or around one of those sites or as a combined diversity at several sites at a time can be assessed.

This process includes the following steps:

a. Generation of a new mutant library (on the gene to be evolved) in which each individual mutant contains either single or multiple mutations located at (or surrounding) a specific active site (a HIT) position detected by the precedent aa-scan process. In the example these mutations include replacement, in each individual mutant, of the native amino acid located either at (or surrounding) the HIT position by one of all other possible amino acids, such that, in the library, and at (or surrounding) each HIT position the native amino acid has been replaced by all possible amino acids.

b. Identification of those mutants that display an increase in protein activity, thus indicating that a new sequence at or surrounding an active site has been identified with higher activity compared to the native sequence. These optimized sequences are named LEADS.”

However, the above cited portion nor the remainder of the specification does not appear to provide support for the limitation/definition “where an optimized lead comprises two or more hit positions”. Note the rejection of “optimized leads” under 35 U.S.C. § 112 2<sup>nd</sup> Paragraph '*VAGUE AND INDEFINITE*' is maintained, since such language remains unclear. Therefore, the above amendment is considered NEW MATTER.

#### **Claims Rejected Under 35 U.S.C. § 112 2<sup>nd</sup> Paragraph**

Claims 1-33 and 42-44 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

#### *VAGUE AND INDEFINITE*

Claim 1 and all claims dependent therefrom are indefinite due to the recitation of a preamble that is different from the actual claimed method steps. The preamble states that it is “A process for the identification of a peptide, polypeptide, or protein that differs in a predetermined property from a target protein...”, however, the claim recites several steps with a final step of

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“(c) individually screening the sets of encoded proteins, whereby one or more proteins that have a predetermined property that differs from the target protein are identified...”. There is no indication in the body of the instant claim that “a peptide, polypeptide” is intended to be identified as recited in the preamble. Therefore, because of the differences between the preamble and actual method steps it is unclear whether the preamble or the method steps set forth in the claims after the preamble control the metes and bounds of the claims. Clarification of the metes and bounds of the claim is requested, via clearer claim wording.

Claim 17 recites the language “optimized lead” which is considered vague and indefinite. The above language implies a set of criteria(s)/parameter(s) that is indicative of an “optimized lead” which is unclear. Clarification of the metes and bounds, via clearer claim language, is requested.

#### **Claims Rejected Under 35 U.S.C. § 102**

The rejection of claims 1-21, 27, and 42-44 under 35 U.S.C. § 102 (e) as being anticipated by Short (U.S. Patent Number 6,171,820 B1) is maintained for reasons of record.

Applicants argue on pages 18 (lines 31-33) and page 19 (lines 7-9) of the ‘*RESPONSE*’, filed 14 March 2005, that the methods disclosed by Short (U.S. Patent Number 6,171,820 B1) are not directed to methods that include individually introducing and screening sets of nucleic acid molecules each encoding a modified protein. Applicants refer to specifically to Example 5 of Short and states that this example does not provide for individual sets of polynucleotides to be individually introduced into host cells in an addressable array.

As previous stated, Short discloses a method of producing a set of mutagenized progeny polynucleotides encoding a polypeptide from a parental template polynucleotide (i.e. target

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protein), via “codon site-saturation mutagenesis”, wherein at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids (instant claims 1, 2, 4, 9-12, and 19-21; Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51). Figure 2 illustrates the use of the site-saturation mutagenesis approach for achieving all possible amino acid changes at each amino acid site along the polypeptide (codon mutagenesis (N,N,G/T); instant claims 13-15 and 42-44; Column 6, lines 47-60). Example 5 describes the screening of the progeny where the mutagenized polynucleotides encoding polypeptides were introduced (i.e. plasmid, viral vector, etc) into host cell (i.e. bacterial) on an addressable array (i.e. well plate, loci, etc) and analyzed for kinetic activities (improved stability/“predetermined property”) (instant claims 3, 5-8, 16-18, and 27; Column 11, lines 38-46; Column 20, lines 51-58; and Columns 55-56, beginning on line 34). The inventor also provides the optional repeating of the described steps (Column 5, lines 8-11). Additionally, the inventors indicate the identification of protein mutational positions (i.e. hit position) (Column 4, line 64 to Column 5, line 34; and Column 12, lines 20-24). Regarding Applicants’ arguments pertaining to “individually introducing” limitation these limitations are not present in the instant claims (i.e. individually introducing). Thus, the rejection of instant claims 1-21, 27, and 42-44 as being anticipated by Short is maintained for reasons of record.

*EXAMINER COMMENT*

In addressing the previous rejection of the term “effected” under 35 U.S.C. § 112 2<sup>nd</sup> Paragraph ‘*VAGUE AND INDEFINITE*’ Applicants have clarified that the term “effected” referred to the commonly used verb form and means “to accomplish”, “to cause come into being”(Refer to page 16, lines 9-10 of the ‘*RESPONSE*’, filed 14 March 2005).

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*ACTION IS FINAL, AS NECESSITATED BY AMENDMENT*

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants' reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

*EXAMINER INFORMATION*

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Examiner Initials: *CGM*

Date:

*June 10, 2005*

*Ardin H. Marschel 6/12/05*  
**ARDIN H. MARSCHEL**  
**SUPERVISORY PATENT EXAMINER**